

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 10787-4/PAR	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 01015	International filing date (day/month/year) 30/08/2000	(Earliest) Priority Date (day/month/year) 30/09/1999
Applicant AUBIN, Jane, E. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of **4** sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01015

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/17 A61K48/00 A61K39/395 A61P19/00 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC:

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, PAJ, WPI Data, MEDLINE, EMBASE, LIFESCIENCES

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VANACKER JEAN-MARC ET AL: "Activation of the osteopontin promoter by the orphan nuclear receptor estrogen receptor related alpha." CELL GROWTH & DIFFERENTIATION, vol. 9, no. 12, December 1998 (1998-12), pages 1007-1014, XP000982519 ISSN: 1044-9523 the whole document --- -/-	1-9, 14, 15



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

23 February 2001

Date of mailing of the international search report

08/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Moreau, J

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01015

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	BONNELYE E ET AL: "The orphan receptor, estrogen related receptor ERRalpha, is differentially expressed during osteoblast development and regulates bone formation." JOURNAL OF BONE AND MINERAL RESEARCH, vol. 14, no. SUPPL. 1, 1999, page S193 XP000982517 Twenty-First Annual Meeting of the American Society for Bone and Mineral Research; St. Louis, Missouri, USA; September 30-October 4, 1999 ISSN: 0884-0431 the whole document ---	1-15
A	BONNELYE EDITH ET AL: "The ERR-1 orphan receptor is a transcriptional activator expressed during bone development." MOLECULAR ENDOCRINOLOGY, vol. 11, no. 7, 1997, pages 905-916, XP000982509 ISSN: 0888-8809 the whole document ---	1-15
A	VANACKER JEAN-MARC ET AL: "Transcriptional targets shared by estrogen receptor-related receptors (ERRs) and estrogen receptor (ER) alpha, but not by ERbeta." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 18, no. 15, 2 August 1999 (1999-08-02), pages 4270-4279, XP002161302 ISSN: 0261-4189 the whole document ---	1-15
P, X	WO 00 47735 A (MCGILL UNIVERSITY) 17 August 2000 (2000-08-17) the whole document -----	9-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/01015

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0047735	A 17-08-2000	AU 2653300 A	29-08-2000

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 13 June 2001 (13.06.01)	
International application No. PCT/CA00/01015	Applicant's or agent's file reference 10787-4/PAR
International filing date (day/month/year) 30 August 2000 (30.08.00)	Priority date (day/month/year) 30 September 1999 (30.09.99)
Applicant AUBIN, Jane, E. et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

02 April 2001 (02.04.01)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41 22) 740 14 36	Authorized officer Claudio Borton Telephone No.: (41 22) 338 83 38
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The demand must be filed directly with the competent International Preliminary Examining Authority or if two or more Authorities are with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line IPEA/ _____

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference 10787-4 PAR
International application No. PCT/CA00/01015	International filing date (day/month/year) 30 August 2000 (30-08-00)	(Earliest) Priority date (day/month/year) 30 September 1999 (30-09-99)
Title of invention ESTROGEN RELATED RECEPTOR, ERR ALPHA, A REGULATOR OF BONE FORMATION		
Box No. II APPLICANT(S)		
Name and address: (Family name followed by given name, for a legal entity, full official designation. The address must include postal code and name of country.) AUBIN, Jane, E. 643 Pape Avenue Toronto, Ontario M4K 3S2 Canada		Telephone No.: (416) 978-4220 Facsimile No.: (416) 978-3954 Teleprinter No.:
State (that is, country) of nationality: CA		State (that is, country) of residence: CA
Name and address: (Family name followed by given name, for a legal entity, full official designation. The address must include postal code and name of country.) BONNELYE, Edith 534, Huron Street Toronto, Ontario M5R 2R7 Canada		
State (that is, country) of nationality: FR		State (that is, country) of residence: CA
Name and address: (Family name followed by given name, for a legal entity, full official designation. The address must include postal code and name of country.)		
State (that is, country) of nationality: 		State (that is, country) of residence:
<input type="checkbox"/> Further applicants are indicated on a continuation sheet.		

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is agent common representative

and has been appointed earlier and represents the applicant(s) also for international preliminary examination.

- is hereby appointed and any earlier appointment of (an) agent(s) /common representative is hereby revoked.
- is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: (*Family name followed by given name; for a legal entity: full official
The address must include postal code and name of country*)

RAE, Patricia, A.
SIM & McBURNEY
330 University Avenue
6th Floor
Toronto, Ontario M5G 1R7
Canada

Telephone No.:
(416) 595-1155

Faxsimile No.:
(416) 595-1163

Teleprinter No.:

Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

the international application as originally filed.

the description as originally filed
 as amended under Article 34

the claims as originally filed
 as amended under Article 19 (together with any accompanying statement)
 as amended under Article 34

the drawings as originally filed
 as amended under Article 34

2. The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). (*This check-box may be marked only where the time limit under Article 19 has not yet expired.*)

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

- which is the language in which the international application was filed.

 which is the language of a translation furnished for the purposes of international search.

 which is the language of publication of the international application.

 which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States (that is, all States which have been designated and which are bound by Chapter II of the PCT)

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|---|---|--------|
| 1. translation of international application | : | sheets |
| 2. amendments under Article 34 | : | sheets |
| 3. copy (or where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter | : | sheets |
| 6. other (specify) | : | sheets |

For International Preliminary
Examining Authority use only
received not received

<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

RAE, Patricia, A.
SIM & McBURNEY

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

The applicant has been informed accordingly.

4. The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No.	PCT/CA00/01015	For International Preliminary Examining Authority use only
Applicant's or agent's file reference	10787-4 PAR	Date stamp of the IPEA
Applicant		
AUBIN, Jane, E. and BONNELYE, Edith		
Calculation of prescribed fees		
1. Preliminary examination fee	2,998.29	P
2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>)	287.51	H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	3,285.80	
	TOTAL	
Mode of Payment		
<input type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash	
<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps	
<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons	
<input checked="" type="checkbox"/> bank draft	<input type="checkbox"/> other (<i>specify</i>): _____	

Deposit Account Authorization (*this mode of payment may not be available at all IPEAs*)

The IPEA/ _____ is hereby authorized to charge the total fees indicated above to my deposit account.

(*this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit*) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

Deposit Account Number

Date (day/month/year)

Signature

Form PCT/IPEA/401 (Annex) (July 1998; reprint July 2000)

LegalStar 2000, Form PCTDFEE

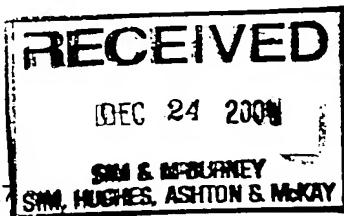
See Notes to the fee calculation sheet

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Rae, P.
Sim & McBurney
330 University Avenue
6th Floor
Suite 600
Toronto, Ontario M5G 1R7
CANADA



PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Applicant's or agent's file reference
10787-4PAR

IMPORTANT NOTIFICATION

International application No. PCT/CA00/01015	International filing date (day/month/year) 30/08/2000	Priority date (day/month/year) 30/09/1999
Applicant AUBIN, Jane, E. et al.		

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Hundt, D

Tel.+49 89 2399-8042



PATENT COOPERATION TREATY

PCT

REC'D 18 DEC 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 10787-4PAR	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CA00/01015	International filing date (day/month/year) 30/08/2000	Priority date (day/month/year) 30/09/1999
International Patent Classification (IPC) or national classification and IPC A61K38/17		
Applicant AUBIN, Jane, E. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 02/04/2001	Date of completion of this report 14.12.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Deck, A Telephone No. +49 89 2399 8432



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01015

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-52 as originally filed

Claims, No.:

1-15 as originally filed

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01015

- the drawings, sheets:
5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application.
- claims Nos. 1-9.

because:

- the said international application, or the said claims Nos. 1-9 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-13

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01015

	No:	Claims	14, 15
Inventive step (IS)	Yes:	Claims	1-13
	No:	Claims	14, 15
Industrial applicability (IA)	Yes:	Claims	10-15
	No:	Claims	see separate sheet

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/01015

Section III:

Claims 1-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V:

1. Reference is made to the following document:

D1: US-A-5840690

The document D1 was not cited in the international search report. A copy of the document is appended hereto.

2. Claim 14 claims a pharmaceutical composition comprising an agent which enhances expression of a gene encoding an ER α protein. According to the description (Example 11), this agent can be estrogen, TGF- β , vitamin D3, among others. These compounds are used in pharmaceutical compositions since a long time.

Claim 15 claims a pharmaceutical composition comprising an ER α antagonist. According to the description (Example 11), this antagonist can be PTH(1-34). This compound is also known to be used in pharmaceutical compositions, see for example D1, claim 9.

The fact that the applicant has discovered one of their mechanism of action does not render new a pharmaceutical composition comprising them.

Therefore claims 14 and 15 do not meet the requirements for novelty of Article 33(2) PCT.

3. The use of an ER α agonist, i.e. antagonist (or other factors which increase, i.e. reduce ER α expression) for increasing, i.e. reducing proliferation or differentiation of osteoblasts, i.e. for treating disorders associated with defective,

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/01015

i.e. unwanted bone formation, is neither described nor suggested in the prior art.

A method of screening for modulators of ERR α is also not described in the available prior art.

Claims 1-13 therefore appear to be novel and inventive.

4. For the assessment of the present claims 1-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VI:

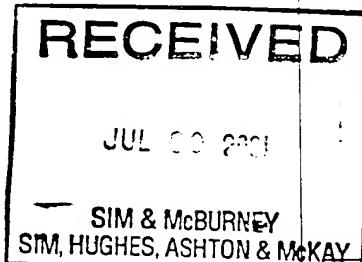
Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-A-0047735	17.08.2000	08.02.2000	08.02.1999

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
Rae, P.
Sim & McBurney
330 University Avenue
6th Floor
Suite 600
Toronto, Ontario M5G 1R7
CANADA



PCT

WRITTEN OPINION

(PCT Rule 66)

		Date of mailing (day/month/year)	27.07.2001
Applicant's or agent's file reference 10787-4PAR		REPLY DUE	within 3 month(s) from the above date of mailing
International application No. PCT/CA00/01015	International filing date (day/month/year) 30/08/2000	Priority date (day/month/year) 30/09/1999	
International Patent Classification (IPC) or both national classification and IPC A61K38/17			
Applicant AUBIN, Jane, E. et al.			

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I Basis of the opinion
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain document cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 30/01/2002.

Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer / Examiner Deck, A
	Formalities officer (incl. extension of time limits) Exner, K Telephone No. +49 89 2399 7826



I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"):

Description, pages:

1-52 as originally filed

Claims, No.:

1-15 as originally filed

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

WRITTEN OPINION

International application No. PCT/CA00/01015

- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c));
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- III. NON-OBVIOUSNESS

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

the entire international application,

claims Nos. 1-9,

because:

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

 - the said international application, or the said claims Nos. 1-9 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
 - the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - no international search report has been established for the said claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- | | | |
|-----------------------------|--------|----------------------|
| 1. Statement
Novelty (N) | Claims | 1, 2, 5, 14, 15 (NO) |
| Inventive step (IS) | Claims | 1, 2, 5, 14, 15 (NO) |

WRITTEN OPINION

International application No. PCT/CA00/01015

Industrial applicability (IA) Claims see separate sheet

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Section III:

Claims 1-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V:

1. Reference is made to the following documents:

D1: VANACKER JEAN-MARC ET AL: 'Activation of the osteopontin promoter by the orphan nuclear receptor estrogen receptor related alpha.' *CELL GROWTH & DIFFERENTIATION*, vol. 9, no. 12, December 1998 (1998-12), pages 1007-1014, XP000982519 ISSN: 1044-9523

D2: US-A-5840690

The document D2 was not cited in the international search report. A copy of the document is appended hereto.

2. Claims 1, 2, 5 encompass the use of an ERR α agonist, for example estrogen (see description, example 11), in the treatment of bone defects. However, estrogen is known for its effect on bone development, see D1, page 1012, right-hand column, third paragraph. Therefore these claims do not appear to be new.

Claim 14 claims a pharmaceutical composition comprising an ERR α agonist. According to the description (Example 11), this agonist can be estrogen, TGF- β , vitamin D3, among others. These compounds are used in pharmaceutical compositions since a long time (see for example the statement in D1, page 1012, right-hand column, third paragraph, that estrogen is used since a long time for bone development in postmenopausal osteoporosis).

**WRITTEN OPINION
SEPARATE SHEET**

International application No. PCT/CA00/01015

Claim 15 claims a pharmaceutical composition comprising an ER α antagonist. According to the description (Example 11), this antagonist can be PTH(1-34). This compound is also known to be used in pharmaceutical compositions, see for example D2, claim 9.

Therefore claims 14 and 15 also do not meet the requirements for novelty of Article 33(2) PCT.

3. The use of an ER α antagonist (or other factors which reduce ER α expression) for reducing proliferation or differentiation of osteoblasts, i.e. for treating disorders associated with unwanted bone formation, is neither described nor suggested in the prior art.

A method of screening for modulators of ER α is also not described in the prior art.

Claims 3, 4, 7-13 therefore appear to be novel and inventive.

4. For the assessment of the present claims 1-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VI:

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-A-0047735	17.08.2000	08.02.2000	08.02.1999

PCT REQUESTOriginal (for **SUBMISSION**) - printed on 30.08.2000 02:27:49 PM

0 0-1	For receiving Office use only International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4 0-4-1	Form - PCT/RO/101 PCT Request Prepared using	PCT-EASY Version 2.91 (updated 01.07.2000)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	Canadian Patent Office (RO/CA)
0-7	Applicant's or agent's file reference	10787-4/PAR
I	Title of invention	ESTROGEN RELATED RECEPTOR, ERR ALPHA, A REGULATOR OF BONE FORMATION
II	Applicant	
II-1	This person is:	applicant and inventor
II-2	Applicant for	all designated States
II-4	Name (LAST, First)	AUBIN, Jane, E.
II-5	Address:	643 Pape Avenue Toronto, Ontario M4K 3S2 Canada
II-6	State of nationality	CA
II-7	State of residence	CA
II-8	Telephone No.	(416) 978-4220
II-9	Facsimile No.	(416) 978-3954
III-1	Applicant and/or inventor	
III-1-1	This person is:	applicant and inventor
III-1-2	Applicant for	all designated States
III-1-4	Name (LAST, First)	BONNELYE, Edith
III-1-5	Address:	534 Huron Street Toronto, Ontario M5R 2R7 Canada
III-1-6	State of nationality	FR
III-1-7	State of residence	CA

PCT REQUEST

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IV-1	Agent or common representative; or address for correspondence The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent RAE, Patricia, A. Sim & McBurney 330 University Avenue 6th Floor Toronto, Ontario M5G 1R7 Canada
IV-1-1	Name (LAST, First)	
IV-1-2	Address:	
IV-1-3	Telephone No.	(416) 595-1155
IV-1-4	Facsimile No.	(416) 595-1163
V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&LI CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
V-5	Precautionary Designation Statement In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	

PCT REQUEST

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V-6	Exclusion(s) from precautionary designations	NONE	
VI-1	Priority claim of earlier national application		
VI-1-1	Filing date	30 September 1999 (30.09.1999)	
VI-1-2	Number	2,284,103	
VI-1-3	Country	CA	
VI-2	Priority document request The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1	
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)	
VIII	Check list	number of sheets	electronic file(s) attached
VIII-1	Request	3	-
VIII-2	Description	52	-
VIII-3	Claims	4	-
VIII-4	Abstract	1	abstract.txt
VIII-5	Drawings	12	-
VIII-7	TOTAL	72	
VIII-8	Accompanying items	paper document(s) attached	electronic file(s) attached
VIII-16	Fee calculation sheet	✓	-
VIII-16	PCT-EASY diskette	-	diskette
VIII-18	Figure of the drawings which should accompany the abstract	2	
VIII-19	Language of filing of the international application	English	
IX-1	Signature of applicant or agent		
IX-1-1	Name (LAST, First)	RAE, Patricia, A.	

FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	
10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
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PCT (ANNEX - FEE CALCULATION SHEET)

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10787-4 PAR

(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only			
0-1	International Application No.			
0-2	Date stamp of the receiving Office			
0-4	Form - PCT/RO/101 (Annex) PCT Fee Calculation Sheet Prepared using	PCT-EASY Version 2.91 (updated 01.07.2000)		
0-9	Applicant's or agent's file reference	10787-4/PAR		
2	Applicant	AUBIN, Jane, E., et al.		
12	Calculation of prescribed fees	fee amount/multiplier	total amounts (CAD)	
12-1	Transmittal fee	T	⇒	200
12-2	Search fee	S	⇒	1,353
12-3	International fee Basic fee (first 30 sheets)	b1	630	
12-4	Remaining sheets	42		
12-5	Additional amount (X)	15		
12-6	Total additional amount	b2	630	
12-7	b1 + b2 =	B	1,260	
12-8	Designation fees Number of designations contained in international application	87		
12-9	Number of designation fees payable (maximum 8)	8		
12-10	Amount of designation fee (X)	136		
12-11	Total designation fees	D	1,088	
12-12	PCT-EASY fee reduction	R	-194	
12-13	Total International fee (B+D-R)	I	⇒	2,154
12-14	Fee for priority document Number of priority documents requested	1		
12-15	Fee per document (X)	0		
12-16	Total priority document fee	P	⇒	0
12-17	TOTAL FEES PAYABLE (T+S+I+P)	⇒	3,707	
12-19	Mode of payment	cheque		
12-20	Deposit account instructions The receiving Office:	Canadian Patent Office (RO/CA)		
12-20-2	is hereby authorized to charge any deficiency or credit any over-payment in the total fees indicated above to my deposit account	✓		
12-20-3	is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account	✓		
12-21	Deposit account No.	000000		
12-22	Date	30 August 2000 (30.08.2000)		

PCT (ANNEX - FEE CALCULATION SHEET)

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12-23	Name and signature	RAE, Patricia, A.
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VALIDATION LOG AND REMARKS

13-2-6	Validation messages Contents	Yellow! The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.
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PCT-EASY INFORMATION SHEET

(For applicant use only, DO NOT submit this sheet with the international application)

VALIDATION LOG

Yellow!	Contents
	The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.

Before submitting the International Application, please carefully verify that:

- the information contained on printed Request form is correct;
- Box IX of the Request form has been signed;
- all elements of the international application as indicated in Box VIII of the Request form have been attached; and,
- the diskette containing the PCT-EASY zip file of the International Application has been enclosed and has been clearly labeled "PCT-EASY", with the applicant's or agent's file reference, and the first applicant's name.

ATTENTION

DO NOT modify any indications on the Request form printout. The attached PCT-EASY application has been locked. If an error or an omission is discovered at this time, you must copy the submitted application as a template and make the change or correction in a new application (using the submitted application as a template). You may create such a template by copying the submitted application from the "Stored Forms" folder to the "New PCT Forms" folder. Open the new (.WO) file created in the "New PCT Forms" folder, correct the errors and proceed with the submission process again.